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Subject: NEWS UPDATES: Despite Industry Concern, EPA Eyes '91 Formaldehyde Risk Value In Rules (Risk Policy Report)
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FYI

Despite Industry Concern, EPA Eyes '91 Formaldehyde Risk Value In Rules

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EPA will likely use its 1991 estimate of formaldehyde cancer risk in ongoing rulemakings until it finalizes an updated estimate accounting for recent criticisms from the National Academy of Sciences (NAS) -- a move that is already drawing concern from industry who fear it will result in stricter requirements than rules EPA has developed based on a controversial industry risk estimate.

The American Chemistry Council (ACC), for example, has already questioned EPA's proposed use of the 1991 risk estimate in an air toxics rule for emissions from pressed wood furnishings, released last December. Agency officials may also rely on the 1991 estimate for development of a host of other emissions rules, including those addressing mobile sources, plywood manufacturers, natural gas turbines, ethanol plants and others, an agency source says.

The NAS' report, released April 8, cast doubts on EPA's draft risk estimate, suggesting that the agency had insufficient evidence to link formaldehyde exposure with leukemia and Hodgkin lymphoma, though the report agrees with EPA's assessment that formaldehyde exposure can cause much rarer cancers of the nose and respiratory tract. In addition, the report reiterated several long-standing concerns with the methodologies employed by EPA's Integrated Risk Information System (IRIS) program, setting back the agency's effort to craft a new risk estimate (*Risk Policy Report*, April 12).

Now, an agency source indicates that EPA will likely resort to using the 1991 risk estimate in ongoing rules where formaldehyde is an issue until the updated analysis is finalized. "EPA is still working off a potency estimate that is 15-20 years old, until such time as we have a final [IRIS assessment,]" the source says. "There are multiple rules out there. Right now, we'll continue to rely on the earlier value."

But that could prove controversial with industry representatives who have already urged EPA to avoid use of the 1991 assessment.

In late February comments, ACC urged EPA to delay its rule on emissions from pressed wood furnishings until the NAS released its report on the agency's updated risk estimate. ACC argued that the 1991 Integrated Risk Information System, (IRIS) risk estimate, which EPA used in the proposed furnishings rule is "an overly conservative and outdated model" that prompted EPA to propose an unnecessarily strict rule for curbing formaldehyde emissions from wood furniture manufacturing facilities. Activists countered that using anything but the IRIS assessment to set the standard would violate the Clean Air Act (*Risk Policy Report*, March 1).

The 1991 estimate has proven controversial because it is more stringent than a formaldehyde cancer risk estimate calculated from a model that the Chemical Industry Institute of Toxicology (CIIT) -- now known as the Hamner Institutes -- developed in the early 2000s.

EPA initially used the 1991 cancer risk estimate in its residual risk rule for emissions from pressed wood furnishings, but later switched to the significantly weaker value calculated using the CIIT model. EPA staff later raised questions about the model in a series of papers, and the air office revised the rule to again base it on the 1991 cancer risk number.

Similarly, EPA also delisted natural gas turbines as a source category subject to air toxic requirements based on the CIIT model.

The three formaldehyde risk estimates could drive greatly varying rules, as the cancer potencies calculated range by some 20,000 times. EPA's most recent draft cancer potency estimate of 1.1×10^{-4} per microgram per cubic meter (ug/m^3) is the most stringent, while the number based on the animal data and the CIIT model is the

10^{-9} m^3

weakest, at 5.5 x 10 per ug/m . The new cancer risk estimate is a factor of 10 stricter than EPA's previous cancer risk estimate, published in 1991, which is set at 1.3 $x10^{-5}$ per ug/m^3.

While the NAS panel faulted EPA's conclusions about the leukemia risks of formaldehyde, the panel appeared to agree with EPA's decision to base the proposed cancer potency estimate on calculations for leukemia, Hodgkin lymphoma and nasalpharyngeal (NPC) cancer.

"The committee agrees that EPA's choice of NPC, Hodgkin lymphoma, and leukemia to estimate the unit risk is appropriate given that the use of Hodgkin lymphoma and leukemia primarily supports the assessment of uncertainty and the magnitude of cancer risk where there is a lack of evidence to support the biologic plausibility of a relationship between formaldehyde exposure and the two cancers," according to the NAS report.

Both the EPA source and an industry source called the contrast confusing. "It really is confusing about what they're trying to say about leukemia," the EPA source says.

An industry source agrees, saying, "I was perplexed by that myself. I don't know how you move forward when you've got no evidence of the link. I didn't understand why they still embraced" the leukemia and lymphoma endpoints EPA used for its cancer risk calculation. "I think it had to do with [the panel] trying to answer the charge questions."

The panel's chair, Jonathan Samet, explains that the reason for such confusion stems from the charge questions put forward by EPA. In this case, the panel was tasked with answering questions such as "review and comment on the scientific support for the choices made in developing the preferred quantitative estimates that are based on dose-response relationships between several cancers and cumulative inhalation exposure, and consider such issues as the appropriate dose metric given the study design, the alternative metrics, and the suitability of alternative metrics for use in evaluating environmental and residential inhalation exposures to formaldehyde," according to NAS' website.

And Samet adds that, "Remember, we're trying to address [the charge] in [EPA's] rules." He added that "if you're going to [calculate a cancer risk estimate], these [endpoints] are the right ones to pick. The point is, if you do it, there's substantial evidence. No other cancers are better."

The NAS report, however, also praises the CIIT model, which is a type of model called a biologically-based dose response (BBDR) model. Such models can be used to estimate a human risk estimate at low doses of exposure from lab animal dose-response data, and are a preferred approach of EPA's.

"Given that the BBDR model for formaldehyde is one of the best-developed BBDR models to date, the positive attributes of BBDR models generally, and the limitations of the human data, the committee recommends that EPA use the BBDR model for formaldehyde in its cancer assessment, compare the results with those described in the draft assessment, and discuss the strengths and weaknesses of each approach."

In its draft residual risk rule on formaldehyde emissions from pressed wood furniture facilities, EPA explains, "In 2004, EPA determined that the CIIT dose-response value for formaldehyde . . . was based on better science than the IRIS dose-response value, and we switched from using the IRIS value to the CIIT value in risk assessments supporting regulatory actions.

This determination was based on a substantial body of research on the inhalation dosimetry for formaldehyde in rodents and primates by the CIIT Centers for Health Research (formerly the CIIT), with a focus on use of rodent data for refinement of the quantitative cancer dose-response assessment. . . . However, recent research published by EPA indicates that, when the CIIT's two-stage modeling assumptions are varied, resulting dose-response estimates can vary by several orders of magnitude. These findings are not supportive of interpreting the CIIT model results as providing a conservative (health-protective) estimate of human risk.

The proposed rule continues, "As a result of these findings, we no longer considered the CIIT URE value health protective, and we are again using the EPA's current value on IRIS, which was last revised in 1991, and which is more than 2000 times greater than the CIIT value. We note that a new IRIS re-assessment has been drafted and sent to the NAS for review. The NAS review is expected to be completed by March of 2011." The rule does not indicate if agency staff will consider the finalized IRIS assessment when finalizing the rule, or if it will await the IRIS assessment.

EPA, however, based IRIS' draft finding that formaldehyde is a human carcinogen and its cancer risk calculations on human epidemiology data -- National Cancer Institute data of some 23,000 workers at 10 different factories where they worked with formaldehyde -- rather than using animal data and the BBDR model. The International Agency for Research on Cancer and the National Toxicology Program also used this data when preparing their monographs on formaldehyde (*see related story*).

An industry source, however, indicates that using the model animal data and the model would yield less strict estimate of risk -- in part because it is based on calculations for nasal tumors but not leukemia or lymphoma.

"They [NAS] came out very strongly on [using] the BBDR for nasal tumors. They said EPA should compare the

risks using realistic assumptions, compute and then compare," the source says. "There is no opportunity to say the same thing for leukemia because there is no [BBDR] model and they are skeptical these [cancers] could even occur [after formaldehyde exposure]." -- *Maria Hegstad*